

From the INTERNATIONAL BUREAU

PCTNOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)

(PCT Rule 44bis.1(c))

To:

Rec'd:FD

SANDERS, Deirdre, E.
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Concord, MA 01742-9133
ETATS-UNIS D'AMERIQUEDate of mailing (day/month/year)
08 June 2006 (08.06.2006)Applicant's or agent's file reference
3518.1024002**IMPORTANT NOTICE**International application No.
PCT/US2004/039589International filing date (day/month/year)
23 November 2004 (23.11.2004)Priority date (day/month/year)
26 November 2003 (26.11.2003)

Applicant

DEPUY SPINE, INC. et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

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JUN 15 2006

HAMILTON, BROOK
SMITH & REYNOLDS, P.C.The International Bureau of WIPO
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

| | | | |
|--|--|--|------------------|
| Applicant's or agent's file reference 3518.1024002 | FOR FURTHER ACTION | | See item 4 below |
| International application No. PCT/US2004/039589 | International filing date (<i>day/month/year</i>) 23 November 2004 (23.11.2004) | Priority date (<i>day/month/year</i>) 26 November 2003 (26.11.2003) | |
| International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237 | | | |
| Applicant DEPUY SPINE, INC. | | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

| | |
|---|---|
| | Date of issuance of this report 29 May 2006 (29.05.2006) |
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland | Authorized officer Athina Nickitas-Etienne |
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 18 JUL 2005

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To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2004/039589

International filing date (day/month/year)
23.11.2004

Priority date (day/month/year)
26.11.2003

International Patent Classification (IPC) or both national classification and IPC
A61P19/10, A61K39/395, A61K45/06

Applicant
DEPUY SPINE, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/039589

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/039589

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-10,89, in respect of IA

because:

- ☒ the said international application, or the said claims Nos. 1-10, 89 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/039589

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-10, 89

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|----------------|
| Novelty (N) | Yes: Claims | |
| | No: Claims | 1-10, 89 |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | 1-10,89 |
| Industrial applicability (IA) | Yes: Claims | |
| | No: Claims | see sep. sheet |

2. Citations and explanations

see separate sheet

Comments on item III

Claims 1-10 and 89 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Comments on item IV

The International Examining Authority considers that the International Application does not comply with the requirements of unity of invention (Rule 13.1, 13.2 and 13.3 PCT) for the reasons indicated in the 'Invitation to pay additional fees' of the International Search Report (ISR).

At present, the search made covers only the first group of inventions among the nine groups found. Hence, the present opinion refers only to the claims belonging to the first group of inventions, i.e., claims 1-10 and 89.

Comments on item V

1. The documents cited in the International Search Report correspond respectively to D1-D8. Any reference to the documents in the present written opinion relates to the passages given in said report, unless otherwise indicated.

D1: EP-A-0 950 417

D2: YAFFE A ET AL: "Combined local application of tetracycline and bisphosphonate reduces alveolar bone resorption in rats" JOURNAL OF PERIODONTOLOGY 01 JUL 2003 UNITED STATES, vol. 74, no. 7, 1 July 2003, pages 1038-1042

D3: US 2003/207827 A1

D4: WO 99/45923 A

D5: CRANDALL C: "Combination treatment of osteoporosis: A clinical review" JOURNAL OF WOMEN'S HEALTH AND GENDER-BASED MEDICINE 2002 UNITED STATES, vol. 11, no. 3, 2002, pages 211-224

D6: EZRA A ET AL: "ADMINISTRATION ROUTES AND DELIVERY SYSTEMS OF

BISPHOSPHONATES FOR THE TREATMENT OF BONE RESORPTION"
~~ADVANCED DRUG DELIVERY REVIEWS~~, AMSTERDAM, NL, vol. 42, no. 3,
31 August 2000, pages 175-195

- D7: NAKAMURA K ET AL: "Stimulation of endosteal bone formation by local
intraosseous application of basic fibroblast growth factor in rats" REVUE DU
RHUMATISME (ENGLISH EDITION) 1997 FRANCE, vol. 64, no. 2, 1997,
pages 101-105
- D8: DESANTIS A ET AL: "Current and emerging therapies in osteoporosis"
EXPERT OPINION ON PHARMACOTHERAPY 2002 UNITED KINGDOM, vol.
3, no. 7, 2002, pages 835-843.

2. As explained in the ISR, both the combination of bone-forming and anti-resorptive agents and its use for treating excess of bone resorption were well known in the art at the date of filing (see D1 to D6). Even though the first approaches to these therapeutic combinations had been done with systemic administration, local delivery to the bone had also been widely disclosed (mainly with biodegradable polymers and osteoconductive materials, see specially D1, D3 and D6).
Reference is made to ISR concerning the specific dependent claims anticipated by each document.
3. For the assessment of the present claims 1-10 and 89 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.